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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/416,920	04/21/95	MILTENYI	EXAMINER 2302000320

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ART UNIT	PAPER NUMBER
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DATE MAILED:

02/21/97

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

### OFFICE ACTION SUMMARY

- Responsive to communication(s) filed on 12/23/96
- This action is FINAL.
- Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 04/3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

- Claim(s) 1-68 is/are pending in the application.
- Of the above, claim(s) 71, 31-33, 52, 57-68 is/are withdrawn from consideration.
- Claim(s) \_\_\_\_\_ is/are allowed.
- Claim(s) 1-30, 34-51, 53-56 is/are rejected.
- Claim(s) \_\_\_\_\_ is/are objected to.
- Claim(s) \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.
- The specification is objected to by the Examiner.
- The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

- Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All  Some\*  None of the CERTIFIED copies of the priority documents have been
- received.
- received in Application No. (Series Code/Serial Number) \_\_\_\_\_.
- received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

- Notice of Reference Cited, PTO-892
- Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_
- Interview Summary, PTO-413
- Notice of Draftsperson's Patent Drawing Review, PTO-948
- Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

15. Applicant's election with traverse of Groups I and II in Paper No. 8 is acknowledged. The traversal is on the ground(s) that are stated in said paper. This is not found persuasive because of the following reasons. Group I is drawn to methods for separating cells, classified in Class 435, subclass 2, group II is drawn to cells, a method for making said cells and kits containing cells, classified in Class 435, subclass 240.1, while group III is drawn to a method of determining secretion of a product, classified in Class 435, subclass 7.1. Because the instant application has been filed under 35 U.S.C. § 371, applicant can elect either invention I and invention II or inventions II and III. Inventions I and III are different methods of use which use different ingredients to achieve different results. Invention I is drawn to methods for separating cells, while invention III is drawn to a method of determining secretion of a product. Invention I uses a cell separation step not used in invention III. Because these inventions are distinct for the reasons given above and the search required for Group I/II is not required for Group II/III and Groups I and III have acquired a separate status in the art as shown by their different classification and divergent subject matter, restriction for examination purposes as indicated is proper. Regarding applicants comments in paper no. 8, the instant application was subjected to restriction under rules for applications filed under 35 U.S.C. § 371, while application 08/441259 was not subjected to restriction under rules for applications filed under 35 U.S.C. § 371, because US application 08/441259 was not filed under 35 U.S.C. § 371.

The requirement is still deemed proper and is therefore made FINAL.

16. Claims 31-33,52,57-68 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 8.

17. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-13,53-56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of copending application Serial No. 08/441259 . Although the conflicting claims are not identical because the scope of claim 1 of 08/441259 differs from that of the instant invention in that it recites that the cells are not lysed as part of the procedure, both sets of claims read on methods that encompass positive selection of cells secreting a particular protein. Therefore, the two sets of claims under consideration in this rejection would have been *prima facie* obvious in view of each other to one of ordinary skill in the art at the time the invention was made for the aforementioned reasons.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. Drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

20. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

21. An application in which the benefits of an earlier application (eg. 07/965,934) are desired must contain a specific reference to the earlier filed application(s) in the first sentence of the specification (37 CFR 1.78).

22. The use of the trademarks SEPHADEX, FICOLL, TWEEN has been noted in this

application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

23. Claims 1-30,34-40,43-50,53-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method or kit which uses a high viscosity or gel forming medium such as gelatin or agarose or alginate, does not reasonably provide enablement for the claimed method or kit that does not use said ingredients. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Manz et al. teach that, "In normal medium the secreted product will readily diffuse away and, in the approach described here, will label all cells covered with the affinity matrix, whether they are secreting or not." (page 1923, first column). Manz et al. later point out that a solution to this problem is to perform the assay in a high viscosity media (page 1923, first column). Thus, Manz et al. establish the need for high viscosity media to practice the instant invention. Therefore, the enablement is not commensurate with the scope of claims that do not recite the aforementioned ingredient as a component of the claimed method or kit.

24. Claims 1-30,34-40,43-50,53-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method or kit wherein antibody or gamma interferon secreting cells are detected, does not reasonably provide enablement for the claimed method or kit for the detection of cells secreting any molecule per se. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims

The specification has not demonstrated that the instant invention can detect any product secreted by cells. Weissman et al. teaches that secreted IL-2 is captured and internalized by high affinity receptors on the cell surface. Therefore, the claimed invention could not be used to detect IL-2 secreting cells, because the IL-2 would have already been captured and removed from the cell surface. This example would apply to any situation where cells with an internalizable receptor

that bind a secreted molecule were present. Therefore, the enablement is not commensurate with the scope of claims that do not recite the aforementioned limitation.

25. Claims 5,6,17,19,20,41,51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 6 lack antecedent basis in claim 1 with regards to the recitation of "label moiety". Claims 17,19 and 20 lack antecedent basis in claim 14 with regards to the recitation of "specific binding partner". Claim 41 lacks antecedent basis in claim 34 in the recitation of "incubation conditions". Claim 41 is indefinite in the recitation of "high viscosity or gel forming" because it is unclear what this means or encompasses other than the specific examples recited in claim 42. Claim 51 is indefinite in the recitation of "cell-cell cross-contamination reducing capture system' because it is unclear what this means or encompasses.

26. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

27. Claims 1-3,14,15,29,30 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Kohler et al.

Kohler et al. teaches the cells and methods of claims 1,14,29,30 (see page 469, section 2.8). The product (eg. IgM) is labelled with a label moiety (eg. with complement) prior to separation.

28. Claims 22 and 23 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Weissman et al.

Weissman et al. teach cells capable of capturing a product secreted and released by said cells wherein the surface of said cells is coupled to a specific binding partner for said product and

wherein the specific binding partner is not a hapten and where the cells are coupled to said product (see abstract).

29. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

30. Claims 1-30,34-40,43-50,53-56 are rejected under 35 U.S.C. § 103 as being unpatentable over Kohler et al in view of Hunt, Segal (US Patent 4,676,980) and prior art disclosed in the specification.

The claims are drawn to a method to separate labelled cells according to a product secreted and released, cells produced by said method and a kit. Kohler et al. teaches a method for labeling and separating cells according to a product secreted and released (see entire document). Kohler et al. teach a method for capturing a product secreted by a cell by labeling the cell with a specific binding partner which captures the secreted product (see abstract). In the procedure taught by Kohler et al. the labelled cell and product are detected by binding of the captured product to complement and subsequent cell lysis. Kohler et al. does not teach that labelled cells are separated using methods other than complement mediated cell lysis. Hunt teaches that labelled cells can be detected using negative selection ( complement mediated cell lysis, pages 55.3-55.4) or positive selection using labelled antibodies (eg. cell sorting based on fluorochrome labelled antibodies pages 55.7-55.13). A routineer would have simply labelled the molecule captured by the method of Kohler et al. with any desired type of label so that it could be positively detected by any art known technique. It would have been prima facie obvious to one of ordinary skill at the time the invention was made to have created the claimed invention because Kohler et al. teach a method for capturing a product secreted by a cell by labeling the cell with a specific binding partner which captures the secreted product and Hunt teaches that labelled cells can be detected using negative selection ( complement mediated cell lysis, page 55.3-55.4) or positive selection (eg. cell sorting based on fluorochrome labelled antibodies 55.7-55.13). Segal teaches bispecific antibodies (see Abstract). Segal teaches that bispecific antibodies can bind a cell surface antigen on the

surface of a target cell and also bind another desired antigen, thus bringing the antigen to the cell surface (see columns 1 and 2). A routineer would used bispecific antibodies which bind any art known molecule that exists on the surface of a desired target cell. The specification discloses on page 14, first paragraph that FACS sorting of labelled cells is known in the art. This procedure involves a fluorescent labelled probe. The specification discloses on page 16, lines 32-35 that methods for separation of magnetic moiety labelled cells are known in the art. A routineer would have used any desired capturing probe instead of TNP, including an antibody and would have attached the antibody to the cell surface using any art known procedure including those utilizing linking agents. The specification discloses on page 10, third paragraph and page 11, first paragraph that attachment of molecules to the cell surface can be achieved via a lipid anchor and a linking moiety. Kohler et al. teach that TNP is connected to the cell surface via an antibody (see page 469, first column, section 2.8). The labelled cells of the invention are produced by the aforementioned procedure. The aforementioned procedure when performed will yield the claimed composition of cells producing a desired product. A routineer would have prepared a kit containing reagents necessary to practice the aforementioned method. The kit would included a high viscosity or gel forming medium because Kohler et al. teach the use of such media (see section 2.8, page 469, first column).

31. No claim is allowed.

32. Papers related to this application may be submitted to Group 180 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 180 at (703) 305-7939.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Tuesday through Friday from 8:30 to 6:00. The examiner can also be reached on alternative Mondays. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general

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nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

*R. Schwadron*

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PRIMARY EXAMINER  
GROUP 1800

Ron Schwadron, Ph.D.

Primary Examiner

Art Unit 1816

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